teaches us that we were often wrong in hypothesizing that an exposure or intervention would only have either a risk-reducing or risk-increasing effect there are many study questions that we would formulate only one-sided. For example, nobody would hypothesize that nuclear power plant workers of the Tschernobyl nuclear power plant who started to clean the site immediately after the accident in 1986 would benefit from the enormous radiation dose that they were exposed to. Furthermore, should we really raise the question whether coronary artery calcification as measured by non-invasive electron-beam computed tomography (EBCT) could have a preventive effect on the risk of coronary artery disease? Or in terms of clinical trials, imagine a situation where a new drug is more toxic than the standard. Efficacy differences in the direction of inferiority of the new drug would be of no interest since the new drug would then clearly be inferior to the standard and the clinical decision would be the same as in the case of no differences.[2] We admit that we should be careful when we formulate one- or two-sided study questions and calculate corresponding one- and two-sided *P*-values. We are also well aware of the danger of *post hoc* abuse, when researchers might be tempted to switch from a two-sided to a one-sided *P*-value when only the one-sided *P*-value would be significant. However, we should not become dogmatic ('always') about the use of either one- or two-sided *P*-values, because it may be in conflict with the original study question and may even prevent scientific progression.

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Are children born to light drinkers not at high risk of developing clinically relevant cognitive–behavioural problems? A response to Kelly *et al.*

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In a study recently published in *IJE*,[1] the authors examined whether there is an association between mothers' light drinking during pregnancy and cognitive–behavioural outcomes in offspring at the age of 3 years. The investigators have conducted the study in two steps: interviewing a large cohort of mothers ($N = 12{,}495$) when their infants were 9 months of age and then assessing the child's cognitive–behavioural functioning at the age of 3 years. The survey at age 9 months was designed to collect detailed information on demographics and maternal health-related behaviours, including maternal drinking during pregnancy. The child's behavioural and emotional problems at the age of 3 years were assessed using the Strengths and Difficulties Questionnaire, and cognitive skills, using the vocabulary subtest from the British Ability Scale (BAS) and the Bracken School Readiness Assessment. Results showed that children born to light drinkers (1–2 drinks per week or per occasion during pregnancy) 'were not at high risk of clinically significant emotional or behavioural problems or cognitive problems'.

While it has been established that heavy drinking, in particular binge drinking, during pregnancy produces a range of morphological anomalies and cognitive dysfunction in offspring,[2] there is no consensus on the issue of whether light drinking has deleterious effects on the developing fetus.[3] This lack of consensus is reflected in the guidelines for drinking during pregnancy published by various professional bodies and government agencies. The Office of the Surgeon General in the USA has urged women who are pregnant or who may become pregnant to abstain from alcohol.[4] This advisory has been adopted by a number of other countries including Canada. Professional organizations such as the Royal College of Obstetricians and Gynaecologists have, however, differed from the above abstinence policies by recommending that women should be careful about drinking during pregnancy and limit consumption to no more than one standard drink a day.[5] Against a backdrop of these differing opinions, Kelly *et al.*'s report that children born to light drinkers are not at high risk for developing adverse cognitive–behavioural

outcomes has significant implications for influencing policy statements regarding drinking during pregnancy. News reports that ensued, carrying headlines such as, 'light drinking in pregnancy may be good for baby boys' (*The Guardian*, Friday, 31 October 2008) and 'light drinking during pregnancy may benefit baby' (foxnews.com, 31 October 2008) have kindled a widespread public interest in the topic of drinking during pregnancy. Therefore, the findings reported in the Kelly *et al*. paper deserve critical examination.

We would like to point out that the study has a number of strengths. First, conducted as a part of the Millennium Study, this investigation has involved a large cohort of women drawn from four regions of the UK. Secondly, the study design has taken into account a wide range of variables that can mediate the effects of prenatal alcohol exposure on the fetus. Despite these strengths, we have two main concerns about the validity of the findings.

First, it seems reasonable to suggest that the authors may have failed to find the effects of prenatal alcohol exposure due to the lack of sensitivity of the test instruments that were employed. A review of neurobehavioural studies of fetal alcohol spectrum disorders (FASD) has revealed that tests assessing fluid reasoning, rapid processing of information, cognitive control and free recall are more sensitive than those assessing simple cognitive processes and recognition memory in detecting cognitive dysfunction associated with prenatal alcohol exposure.[6] We found that a test of fluid reasoning discriminated alcohol exposed and control groups better than a test of recognition vocabulary.[7] While the child's vocabulary reflects his or her general cognitive ability, it also heavily depends on the language input. Huttenlocher[8] obtained evidence that the growth of vocabulary and syntactic skills was closely related to the speech the child heard at home and school. Standardized test instruments and well-established experimental procedures to assess the emerging skills in cognitive control and response inhibition are now available. It is reasonable to suggest that the child's school readiness skills, as assessed by the Bracken tests, are also largely dependent on his or her environment. The authors caution about the reliability of the data gathered through the Strengths and Difficulties Questionnaire as the multi-informant format was not used. Furthermore, the environment of pre-school age children is highly structured by adults and, consequently, alcohol-affected children with subtle central nervous system (CNS) damage may not show difficulties in behaviour regulation until they are older. Consistent with this observation, the evidence from animal models of prenatal alcohol exposure shows that rats exposed to light to moderate amounts of alcohol prenatally display deficits in learning and memory only when they are challenged by demanding tasks.[9]

Secondly, even if the authors had used sensitive tests to assess cognitive functioning in alcohol-exposed children, one could still justifiably raise a question about the generalizability of the results. It has been established that the effects of prenatal alcohol exposure is moderated by a range of variables such as mother's age, body mass and health habits.[10] Given that children born to light drinkers did not display delays in language development, had acquired age appropriate school readiness skills and were not rated as having clinically significant behavioural problems, one could assume that the majority of these children perhaps came from relatively stable families with educated parents. It is possible that the mothers of these children had their drinks with meals, perhaps a glass of wine with dinner. A comparison of morphological anomalies resulting from prenatal alcohol observed in Italy and South Africa revealed that the Italian children were less affected than the South African children by the exposure to the same amount of alcohol.[11] This difference was attributable to a number of socio-cultural factors including drinking patterns. Evidence from animal studies suggests that deleterious effects of alcohol interact with the type of drink, e.g. less harmful effects from red wine than other drinks.[12] Therefore, one can speculate that anti-oxidants in wine may mitigate the harmful effects of ethanol on the fetus. Thus, the results from the Kelly *et al*. study may not be generalizable to a population of women who are malnourished, who may have smaller body masses and who drink beer or hard liquor with a group of friends over the weekend.

In view of the above concerns, one cannot use the results of the Kelly *et al*. study to support a policy statement such as light drinking during pregnancy is safe. In our view, abstinence from alcohol remains the safest practice for a woman who is pregnant or who plans to be pregnant.

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